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## *NEW CONCEPTS IN FAT METABOLISM*

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# *NEW CONCEPTS IN FAT METABOLISM*

By RUTH WOODS

During normal times the average person in the United States consumes about one hundred pounds of fat each year. This amount represents about one-third the entire caloric intake of the diet. About one-half of this is the so-called "invisible" fat naturally contained in foods, chiefly meats and dairy products other than butter. The remainder is "visible" fat such as butter, lard, peanut butter, margarines and various cooking fats and oils.

One of the major roles of fat in the diet is as a source of calories. Fats also contribute significantly to the satiety value of the diet and have an important psychological appeal because of the flavors and odors associated with them. Fats possess a number of important functions not associated with their caloric contributions. These include the influence of fats and their component fatty acids on other constituents of the diet, their role as vehicles for naturally-occurring fat-soluble vitamins and other essential fat-soluble materials, and the specific biological functions associated with the group of so-called essential fatty acids.

The digestion, absorption and subsequent oxidation of fats have been the subject of extensive investigations during the past thirty years. Many of the long-established concepts in this field have been modified as a result of recent studies and new techniques of investigation. Particularly interesting are the newer findings with respect to the digestibility and rate of absorption of fats, the dynamic equilibrium of body fat and the interrelationships between fat and other dietary components. The present Review will be limited to these aspects of fat metabolism. The functions of the essential fatty acids and the effect of lipotropic compounds on fat deposition will be discussed in this publication at some future date.

## *Digestibility:*

Contrary to popular opinion, commonly used fats rank high in digestibility. In an ordinary mixed diet, for example, 95 per cent of the fat eaten will be digested, as compared to 98 per cent of the carbohydrates and 92 per cent of the proteins (1). Fats are more slowly evacuated from the stomach than are proteins and carbohydrates and require more time for absorption. Distinction must be made, however, between the relative slowness of digestion and absorption, and the actual degree of digestibility. In fact, although rapidity of digestion of foods in general is often thought desirable, it is recognized that the slower digestion of fat may possess certain distinct advantages. Prolonged stay in the stomach prevents too early return of hunger, increases the satiety value of small meals, extends the absorption of glucose over several hours, and reduces excessive intestinal motility.

The digestibility of fats is influenced by at least four general factors:

1. The species of the animal ingesting the fat.
2. The health and age of the animal.
3. The amount of fat in the diet.
4. The chemical and physical characteristics of the fat.

It has been found that in many, but not all, instances a fairly close correlation exists between the utilization of fat by rats and by man, so that laboratory findings with this experimental animal are of value in judging the usefulness of a fat to man. With respect to age, it is noted that infants, particularly premature infants and twins, often have a very low tolerance for fats which are ordinarily well digested by adults. The digestibility or absorption of fats is interfered with in certain disorders such as intestinal catarrh, obstructive jaundice, pancreatic deficiency, sprue and celiac disease. The fat level of the diet, as it increases up to a certain optimal level, favorably influences fat digestibility. Recent studies have shown that high levels of protein likewise promote digestibility of accompanying fats (1a). With respect to physical and chemical properties as factors influencing digestibility of fats, numerous studies have been conducted over the past thirty years. These involve every aspect of the subject including actual type of fat (lard, butterfat, coconut oil, etc.), effect of emulsifying agents such as lecithin, hardness and melting point of the fat, degree of unsaturation, fatty acid composition and glyceride structure.

Before elaborating upon this prominent phase of the investigations on fat digestibility, it may be helpful to review briefly some basic facts in the chemistry of fats:

Fats are esters of fatty acids with glycerol. These are known as glycerides or, more specifically, triglycerides because each glycerol molecule is combined with three fatty acid molecules. Triglycerides in which the three fatty acid radicals are of the same kind are known as *simple triglycerides* (tristearin, triolein, tripalmitin). A *mixed triglyceride* is one in which the fatty acid radicals are not all of the same kind. Examples are distearo-olein (having two radicals of stearic and one of oleic acid), dioleo stearin (having two radicals of oleic and one of stearic acid), and stearo-oleo-palmitin (having one radical each of stearic, oleic and palmitic acids).

The characteristics of a fat are dependent upon its total fatty acid composition, its glyceride structure, and upon certain other substances which may be associated with the glycerides as impurities or part of the lipid molecule (2).

The fatty acids may be grouped into a few homologous series, each group possessing a basic general formula, the individual members differing in the length of the carbon chain.

The fatty acids may also be classified as saturated or unsaturated depending upon the type of carbon linkage in the molecule. The unsaturated fatty acids contain one or more "double bond" links which means that the compound can take up additional hydrogen to form a saturated compound. The melting points of an

unsaturated fatty acid and of the corresponding fat or oil are lower than those of a saturated fatty acid and its corresponding fat. Thus the saturated 18 carbon stearic acid melts at 69° C. and stearin at 54° C., while the unsaturated oleic acid, having the same number of carbons, melts at 14° C. and olein at —17° C.

**Type of Fat:** Experiments have been conducted with animals and human beings on the relative digestibility of various common fats such as butterfat, beef fat, mutton tallow, cocoa butter, corn oil, soybean oil and coconut oil. About twenty years ago, Langworthy and Holmes (4, 5, 6) reported the results of a series of such experiments with human adult subjects in which they found the following coefficients of digestibility: Butterfat 97, beef kidney fat 88, coconut oil 98, cocoa butter 95, corn oil 97 and soybean oil 97.5 percent. More recent studies on some of these same fats as digested by rats were reported by Hoagland and Snider in 1943 (7). Soybean oil, corn oil and coconut oil were highly digestible, followed by butterfat, oleo stock, mutton tallow and cocoa butter.

**Level of Fat in Diet:** In these same experiments by Hoagland and Snider, it was found that increasing the level of fat in the diet from 5 to 15 per cent by weight had little effect on the digestibility of soy, corn and coconut oils; slightly improved the digestibility of butterfat, and markedly improved the digestibility of oleo stock, mutton tallow and cocoa butter.

**Melting Point:** The influence of melting points and hardness of fats upon their digestibility has been the subject of extensive investigation during the past three decades. This has been clearly demonstrated in the extensive tables published by Langworthy (8) on the retention by human subjects of twenty-three animal fats, thirty-four vegetable fats and six hydrogenated oils. Digestibility fell below 90 per cent for only those fats which melt at points above 50°C. and are known to contain large amounts of stearic acid. During these and other investigations an inverse relationship has always been observed between increase in melting point and digestibility. This has been interpreted as meaning that the melting point is a direct factor in determining digestibility. Hoagland and Snider (7), however, found that in their experiments no consistent relationship could be demonstrated between the melting points of the various fats and their digestive coefficients. The superior digestibility of fats of low melting point was thought to be due to their more ready emulsification. More recently, however, evidence has been presented which indicates that a more accurate factor in determining digestibility may be the glyceride structure of a fat.

The interrelationships between melting point, glyceride structure and digestibility are very complex. With pure simple triglycerides the melting point is *directly* dependent upon fatty acid composition and its correlation with digestibility can be strikingly demonstrated (2). In ordinary mixed

fats, however, the melting point depends not only on the quantitative fatty acid composition but on actual glyceride structure and does not correlate directly with digestibility.

**Stearic Acid Content:** Two years ago, Mattil and Higgins (8, 9) published some observations on the effect upon digestibility of actual glyceride structure. They were able to demonstrate an inverse relationship between digestibility of fats and stearic acid content. The term "stearic acid" is meant to include not only stearic acid itself, but all members of the stearic (saturated) acid series with eighteen or more carbons atoms.

They fed rats synthetic glycerides composed of one or more molecules of stearic acid in combination with one or more molecules of oleic acid. Their results indicated quite clearly that stearic acid is poorly digested whether fed as a mixed glyceride or as a simple triglyceride.

The degree of digestibility of stearic acid was found to be dependent upon several factors. When it was present as the sole source of fat (tristearin) in the diet of rats it was digested and metabolized in order to fulfill energy requirements. When, however, a more desirable glyceride such as triolein is fed along with tristearin, the rat attempts to meet his needs with as little stearic acid as possible. It was further noted in these studies that when it was essential for the rat to draw upon stearic acid to meet energy requirements, the stearic was more digestible when fed as mixed triglycerides containing oleic acid than when fed as tristearin mixed with triolein.

Mattil and Higgins conclude that if the diet contains one of the customary edible fats, essentially all of the tristearin and most of the other stearic acid in the fat would not be digested, provided that the dietary requirements of the rat were met by other more desirable fatty acids.

Similar conclusions as to the influence of stearic acid content on the indigestibility of a fat may be drawn from the experiments of Hoagland and Snider (10). They determined the digestibility in rats of various higher saturated fatty acids as the free acids and as the corresponding triglycerides when blended with olive oil. The olive oil alone was 97.4 per cent digestible, but the mixtures containing tristearin and trimyristin (composed of a 14-carbon acid) were so poorly absorbed that the tristearin was estimated to be only 6 or 8 per cent and the trimyristin 82 to 84 per cent digestibile when they constituted 5 to 10 per cent of the mixture. Adding 25 per cent stearic acid to olive oil reduced the digestibility from 97.4 to 76.5. The saturated fatty acids of shorter chain length than stearic were well absorbed.

From these and other related studies, modern investigators conclude that the digestibility of fats depends more upon the amounts of longer-chain saturated acids than upon the total saturated acids. It is believed, therefore,

that if fats are hydrogenated in such a manner as to produce a considerable amount of stearic acid, their digestibility will fall and their total food value be reduced in the same proportion.

**Oleic Acid:** In a series of studies with rats on the growth-promoting properties of various glyceride fractions separated from milk fat, Jack, Henderson, Reid and Lepkovsky (11) found evidence to the effect that either the oleic acid content or the total unsaturation might be a factor contributing to the better growth response obtained with fats of different compositions. This conclusion, coupled with the effect of oleic acid in improving the digestibility of stearic acid in a mixed glyceride (8) leads to the hypothesis that just as stearic acid may be a limiting factor, oleic acid may very likely be a positive factor in determining the degree of digestibility of a given fat.

## *Fat Absorption:*

The subject of fat absorption from the small intestine is one which has received an equal amount of prolonged and extensive investigation as has that of fat digestibility. Since much of the material in connection with this subject is beyond the scope of this Review, the present discussion will be limited to one or two aspects which link rate of absorption with digestibility.

The rate of absorption of a fat is an important factor in its nutritive value. For example, it is possible that a fat which is almost completely digested over a given length of time, might nevertheless have a slow rate of absorption through the intestinal wall. Since the fat is present in the intestinal tract for a certain limited period of time, it is apparent that the amount available to the body may be reduced because of the slowness of absorption, even in a fat of high digestibility. Here again, the question of the influence of melting point arises, for it has been shown that this is one of the factors involved in determining rate of absorption. In general it has been found that both digestibility and absorption fall off markedly with fats which melt above 50°C. (12, 13, 14). Inasmuch as the higher melting points of fats are usually associated with an increased proportion of tristearin, it is difficult to distinguish between the influence on digestibility of the melting point *per se* and of the stearic acid content.

In an interesting study by Augur, Rollman and Deuel (15) the effect of lecithin in stimulating the rate of absorption and coefficient of digestibility of fats has been demonstrated. The explanation for the action of lecithin is based on its emulsification properties. Whether fats are absorbed as extremely finely emulsified neutral fat according to the partition theory of Frazer (16) or as fat which must first undergo lipolysis, the promotion

of emulsification by lecithin is obviously an important factor. In the first case absorption of fat is speeded up through improved emulsification and digestibility of the less readily utilized fats. In the light of the lipolytic theory, it might be assumed that the presence of lecithin would again increase the speed of absorption by providing a greater emulsification which, in turn, would permit a more rapid action of the lipolytic enzymes.

Of practical interest in view of these considerations is the possibility that finely emulsified fats such as are present in homogenized milk, ice cream and evaporated milk, may be more readily digested.

## *Dynamic Equilibrium of Body Fat:*

Through the isotope technique which permits the "tagging" of test compounds so that their metabolic pathways can be traced, a number of new concepts were introduced into existing theories of fat metabolism (17).

In mammals most of the fat is deposited under the skin, between muscles or around internal organs. This fat is known as storage or depot fat and was generally regarded as being essentially inert, constant in composition and drawn into metabolic processes only under stress of emergencies such as starvation. Energy was thought to be derived directly from dietary fat and other food constituents; of which excess supplies were relegated to the inert deposits of storage fat.

About twelve years ago, Schoenheimer, Rittenberg and their associates (18) fed fats tagged with deuterium ("heavy" hydrogen) to rats, sacrificed the animals after a few days and analyzed the body fat for the presence of the deuterium. They found that almost half of the tagged dietary fat (44%) had found its way into the "inert" storage fat, yet the total fat reserves remained constant! This could only be interpreted as an indication of rapid and constant fat replacement. The implication was obvious — an amount of depot fat corresponding to that newly deposited must have been degraded and utilized. In other words, the fats which the animals burned were not merely the absorbed dietary fats, but consisted of an almost equal mixture of ingested food fats and storage fats. These and subsequent studies soon brought to light the new well-recognized fact that the so-called "inert" stores of fat are in a state of constant, rapid flux and that dietary fat and depot fat are in continuous dynamic equilibrium.

Other experiments with single, pure tagged fatty acids (19) offered conclusive evidence for the biological desaturation and conversion of one fatty acid into others. They also indicated that this interconversion of fatty acids occurs in the body even if the fatty acids formed are supplied plentifully in the diet as, for example, with the inclusion of butter.

Further experiments (20, 21) showed that fats can be synthesized in the body from other dietary materials (such as carbohydrates) and that this formation is a continuous and rapid process irrespective of the presence or absence of dietary sources of fat.

It is now recognized that all the lipids of the fat depots are constantly subject to a great variety of highly complex chemical processes — synthesis, interconversion and degradation. Schoenheimer (17) concluded:

> "The fatty acids of the depot fat are to be regarded as being constantly transported, in the form of fats or phosphatides, to and from the organs, where fatty acids are temporarily liberated by rupture of ester linkages. When fat is absorbed, the acids of dietary origin merge with those from the depot, thereby forming a mixture indistinguishable as to origin. Parts of the liberated acids are converted to others, while new ones are steadily formed by condensation of small molecules derived from other substances. Some of this pool of acids is degraded, and some of it re-enters ester linkages to regenerate fat, then transported back to the depots. All these complex reactions are so balanced that the total amount and structure of the fat mixture in depot, blood, and organs remain constant."

## *Interrelations Between Fats and Other Nutrients:*

The fat level of the diet as well as the specific fatty acid composition of the dietary fats have been observed to play an important role in the utilization of the various vitamins, particularly of vitamin A and thiamine. Rancidity in fats may be a factor in the destruction of other dietary components and is an important consideration in practical feeding problems. The influence of various vitamins and lipotropic factors upon fat and phospholipid formation, rate of turnover and deposition in the liver constitutes another engrossing chapter in the story of fat metabolism which will be considered separately in a future issue.

**Utilization of Carotene and Vitamin A:** In 1940, W. C. Sherman (22) reported some observations on the effect of the fatty acid composition of the diet on the utilization of the pro-vitamin A, β-carotene. He found that rats kept on a low-fat, vitamin A-free diet until eye lesions and cessation of growth were manifested, showed a superior growth response to low levels of β-carotene when it was fed with certain purified oils than when it was fed alone. Best growth responses were obtained with oils high in unsaturated fatty acids. Those fats which were too low in unsaturated fatty acids to protect against scaliness* in the animals had no effect upon growth. Accordingly, further tests were made with the addition of linoleic acid in the form of methyl linolate. Surprisingly, it was found that when methyl lino-

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*A manifestation of a dietary deficiency of the group so-called "essential fatty acids," particularly of linoleic acid.

late was fed with low levels of carotene, the scaliness was cured but the vitamin A deficiency was intensified! This interference of methyl linolate with carotene utilization was prevented by the addition of soy bean oil or by feeding the two supplements (i.e., methyl linolate and carotene) several hours apart in which case the methyl linolate improved the growth. Growth was also increased by methyl linolate when fed with larger amounts of carotene. Methyl linolate did not cause direct destruction of the carotene prior to its ingestion by the rats nor did it decrease the efficiency of absorption of carotene. It is believed, therefore, that linoleic acid interferes with the metabolism of carotene or vitamin A and that certain oils contain factors which protect against this interference.

The following year an interesting study was reported by Russell and co-workers (23) on the effect of fat level of the diet on the absorption and retention of carotene and vitamin A by hens. On a low fat (0.1 per cent or less) ration laying hens absorbed less crystalline carotene than on a normal ration containing about 4.0 per cent fat. Further, when the level of carotene feeding on the normal ration was increased four-fold, the quantity of carotene retained showed an increase of the same order. On the low fat ration, however, there was only a two-fold increase and the quantity of carotene retained was markedly less than with the normal ration. With vitamin A, however, hens seemed to absorb this material as efficiently on low fat rations as on the normal, but apparently do not retain the vitamin as well without fat, as evidenced by post mortem examinations of the livers.

Studies by other investigators (24, 25) have contributed to the evidence that both carotene and vitamin A, the former particularly, (26) are more completely absorbed if the diet contains a higher percentage of fat.

The presence of rancid fats in the diet may exert a deleterious effect upon vitamin A by oxidative destruction. This may be explained by the presence in rancid fats of peroxide linkages which act as oxidizing agents. This action of rancid fats on vitamin A is of considerable practical importance. It is well known, that, in mixed animal feeds, the added vitamin A disappears rapidly under conditions of warehouse storage. This is particularly true for vitamin A added in the form of fish oils or their concentrates (27). Refining processes often remove a large portion of the protective antioxidants of oils. Such refined oils are prone to oxidation with concomitant destruction of the fat soluble vitamins (vitamins A and E and, to a lesser extent, vitamin D).

**Other Fat-Soluble Vitamins:** Vitamin E is particularly sensitive to oxidation and may be entirely destroyed in a mixed diet by the inclusion of rancid fat. In fact this is one of the common methods for preparing vitamin E-free diets for experimental purposes. Hove *et al* (28) also have demon-

strated that vitamin E extends the effectiveness of suboptimal quantities of linoleic acid in preventing or curing the deficiency syndrome in the rat associated with a lack of linoleic acid.

Vitamin D is less sensitive to rancidity oxidation than the other fat-soluble vitamins. The antirachitic effect of the vitamin has been shown to be enhanced by the presence of non-rancid dietary fat and, under the same conditions, the retention of calcium and phosphorus are increased (3).

Vitamin K has been shown to be destroyed by the presence of the fatty acid, dihydroxystearic acid, a possible product of rancidity. Feeding vitamin K treated with this acid causes an actual vitamin K deficiency in rats as manifested by the development of extensive hemorrhages (29). The loss of the fat-soluble vitamins, particularly A and D, through the inclusion of non-absorbed fat solvents such as mineral oil (25) is another significant relationship which is of practical importance in human nutrition.

**Dietary Fat and Thiamine:** Of all the effects of fat on other nutrients, perhaps one of the most widely studied has been that on the so-called vitamin $B_1$ sparing action. Evans and co-workers (30, 31) pointed out almost fifteen years ago that the intake of vitamin $B_1$ could be greatly reduced if the diet was rich in fat. Since that time numerous studies on the subject have been reported, all demonstrating that the effect is due to fat *per se*. Accordingly, energy requirements can be met by an alternative metabolic route, namely the oxidation of fat rather than of carbohydrate. This diminishes the total thiamine requirements of the body and leaves available a relatively larger amount of this vitamin for other purposes. The very striking effect of changing from a thiamine-free high carbohydrate diet to a thiamine-free high fat diet was demonstrated some years ago by Stirn, Arnold and Elvehjem (32). Animals declining rapidly responded to the administration of fat in the same way as those fed curative doses of thiamine! With a diet rich in fat, all external symptoms of polyneuritis are apparently prevented and good growth results. With as little as 25 per cent of fat in the diet, investigators have shown that almost optimal growth rates can be attained with only 20 per cent of the vitamin B complex supplements usually fed rats on high carbohydrate diets. The thiamine sparing action of fat has been explained on the basis that co-carboxylase (the thiamine-containing enzyme) is needed for carbohydrate but not for fat metabolism.

Another aspect of the thiamine-fat interrelationship is the theory that vitamin $B_1$ is necessary for the synthesis of fat from carbohydrate. This theory was advanced about ten years ago by McHenry (33, 34, 35) and seemed to be generally accepted (36, 37) until recently when some question was raised as to the specificity of thiamine in this reaction.

This role of thiamine in fat synthesis has been questioned, however, by at least two groups of workers. Quackenbush *et al* (38) pointed out that in the experiments of McHenry's group, thiamine feeding was preceded by a two to three week period of depletion on a diet deficient in the entire B complex and therefore suggest that the observed increases in fat synthesis might not be due to a specific action of thiamine *per se,* but to a general improvement in the nutritive state of the animal brought about by the thiamine.* Accordingly Quackenbush and his group conducted similar studies in which they determined the response to water-soluble vitamin supplements after long periods of depletion on two types of low fat diets. The first of these was deficient primarily in thiamine; the second contained ample thiamine but was deficient in other B complex vitamins. They found that thiamine did not prevent rapid losses of total fat in rats on a diet deficient in other B vitamins, nor did thiamine appear to be more effective than other B vitamins in increasing total fat content of the animals. They conclude that "the effectiveness of a supplement in restoring normal fat synthesis in deficient rats is apparently determined by the completeness with which it supplies essentials lacking in the body tissues as well as in the basal diet."

An attempt to further elucidate the problem by means of the isotope technique was made a few years ago by Boxer and Stetten (39). They maintained three groups of young rats on a high carbohydrate, fat-free diet, with the following provisions: Group A, nutritionally complete diet offered *ad libitum;* Group B, thiamine-deficient diet offered *ad libitum;* Group C, nutritionally complete diet restricted in quantity to the amount consumed by Group B. Group B, exhibiting failure of appetite as a result of thiamine deprivation consumed less than Group A.

Isolation from the animal bodies of the newly synthesized "tagged" fatty acids revealed much less formation of fatty acids in Groups B and C than in A. The authors conclude, therefore, that the decrease in fat content in rats on thiamine-deficient diets results from a failure to synthesize and deposit fatty acids. They interpret this failure as being attributable chiefly to the diminished food intake rather than to any specific action of thiamine.†

## *Conclusion:*

The role of the fats in nutrition has been sketched briefly, demonstrating their important caloric and satiety value, their psychological appeal to appetite and their functions as carriers of fat-soluble vitamins, as the only

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*Ed. Note: Although the animals were on a preliminary diet devoid of the entire B-complex, supplementation during the test period consisted only of thiamine without the other members of the vitamin B complex.

† In this connection, it should be pointed out that McHenry also conducted experiments with isocaloric controls designed to eliminate the food intake factor.

dietary source of the essential fatty acids and as factors aiding in the absorption and utilization of various vitamins and minerals.

In the light of current theories of fat digestibility, new practical aspects of the problem of fat hydrogenation have to be considered. It is generally believed that hydrogenation, if excessive in degree, may be carried to a point where digestibility may be reduced and the essential unsaturated fatty acids eliminated. Consideration must also be given rancidity as a factor involved in the destruction of the nutritive properties of a fat or of feeds in which such fats may be incorporated. As Burr (3) has remarked, all processing should be so conducted that fats reach the consumer in a fresh and palatable condition and as unimpaired as possible in dietary essentials.

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